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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,159	06/27/2001	Shigeru Kawahara	206269US0PCT	9776

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EXAMINER
ZUCKER, PAUL A

ART UNIT	PAPER NUMBER
1621	11

DATE MAILED: 09/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/830,159	KAWAHARA ET AL.	
	Examiner	Art Unit	
	Paul A. Zucker	1621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *28 June 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Current Status

1. This action is responsive to Applicants' amendment and declaration of 28 June 2002 and 29 June 2002 in Papers No 10 and 11, respectively.
2. Receipt and entry of Applicants' amendment is acknowledged.
3. Applicant's cancellation of claims 1-4 is acknowledged.
4. Applicant's addition of new claims 5-15 is acknowledged.
5. Claims 5-15 remain outstanding.
6. The objection to the specification set forth in paragraph 1 of the previous Office Action in Paper No 8 is withdrawn in response to Applicant's amendment.
7. The rejections under 35 USC § 112, second paragraph, set forth in paragraphs 2 - 4 of the previous Office Action in Paper No 8 are withdrawn as moot in view of Applicants' cancellation of all original claims.
8. The rejection under 35 USC § 102/103 set forth in paragraph 5 of the previous Office Action in Paper No 8 is withdrawn as moot in view of Applicants' cancellation of all original claims.
9. The rejection under 35 USC § 103 set forth in paragraph 6 of the previous Office Action in Paper No 8 is withdrawn as moot in view of Applicants' cancellation of all original claims.

New Rejections

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 5 –9 and 11 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Claude et al (US 5,510,508 04-1996).

Claude discloses (Column 4, lines 18-26) a process for the crystallization of N-[N-(3,3-dimethylbutyl)-L—aspartyl]-L-phenylalanine methyl ester (Neotame) from water-methanol solution which contains little or no methanol. The claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable.

In the alternative, the invention as a whole is obvious over the disclosure of Claude since it provides no patentable modification of the process as disclosed by Claude:

recrystallization of Neotame from a water-methanol solution at a temperature around 40°C.

Instantly claimed is a method for the crystallization of N-[N-(3,3-dimethylbutyl)-L—aspartyl]-L-phenylalanine methyl ester (Neotame) to obtain crystals having a specified set of characteristic peaks. Claude further discloses (Column 4, line 19) that crystallization is carried out below 40°C.

Claude teaches (Column 4, lines 18-26) a process for the crystallization of N-[N-(3,3-dimethylbutyl)-L—aspartyl]-L-phenylalanine methyl ester (Neotame) from water-methanol solution which contains little or no methanol. Claude is silent with respect to the exact amount of methanol in solution but indicates that methanol is removed by evaporation and thus a low concentration or absence of methanol (cf. instant limitation in claim 2 of "15 wt.% or less" methanol content) can be assumed. Claude further teaches (Column 4, line 19) that crystallization is carried out below 40°C. This is within 10°C of the temperature of 30°C claimed as a lower limit in the instant case (Claim 9). It is therefore reasonable to assume that crystallizations performed at 35 °C, for example, under the conditions described by Claude will have the same diffraction characteristics as those claimed in the instant application. The claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. Small adjustments in solvent ratios in the solvent composition disclosed by Claude to achieve the optimum result

from the crystallization process would be well within the skill of one of ordinary skill in the art.

Thus the instantly claimed process would have been obvious to one of ordinary skill in the art. The motivation would have been to purify Neotame, a compound used as an artificial sweetener for human consumption. The expectation for success would have been high since the starting material, solvent composition and product are the same as that taught by Claude.

Claim Rejections - 35 USC § 103

11. Claims 12-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Claude et al (US 5,510,508 04-1996), and further in view of Tosoh et al (WO 93/02101 02-1993).

Instantly claimed is a method for the crystallization of N-[N-(3,3-dimethylbutyl)-L—aspartyl]-L-phenylalanine methyl ester (Neotame) to obtain crystals having a specified set of characteristic peaks. Further claimed is the use of seeding to generate the desired crystalline form.

Claude teaches (Column 4, lines 18-26) a process for the crystallization of Neotame from water-methanol solution which contains little or no methanol. It is therefore assumed that crystallizations under the conditions described by Claude will have the same diffraction characteristics as those claimed in the instant application.

The method of Claude differs from the instant method in that Claude is silent with regard to the use of seeding to generate the desired crystalline form. Such use of seeding, however, is standard practice in a crystallization experiment when seed crystals are available.

Tosoh, in fact, teaches (Page 4, lines 5-1) the use of seeding to preferentially form crystals of aspartame having the desired properties. Aspartame is an artificial sweetener very closely related in structure and properties to Neotame. Neotame can, in fact, be synthesized from aspartame in a single step. Tosoh's teaching demonstrates the well understood principle in organic chemistry that a preferred type of crystal can be obtained by seeding with that type of crystal. The invention outlined in claims 12-15 simply represents the application of standard laboratory practice to a previously disclosed process for producing crystals of Neotame, presumably having the required crystalline form.

Thus the instantly claimed process would have been obvious to one of ordinary skill in the art. The motivation would have been to purify Neotame, a compound used as an artificial sweetener for human consumption. The expectation for success would have been high since the starting material, solvent composition and product are the same as that taught and seeding-a commonly used technique in crystallization experiments -was employed.

Response to Applicant's Arguments with Regard to These Rejections

12. Applicant's declaration has been fully considered but is not considered persuasive because Applicant presents only selected peak values from the powder x-ray diffraction spectra of Applicants' A type crystal. The complete spectra of both the A type crystal and the prior art crystal must be provided in order to allow for a side-by-side comparison and determination of patentability over the prior art crystal.

13. Applicant has put forth several arguments with regard to these rejections. The Examiner responds below to each of these in turn:

With regard to the rejection of claims 5-11 Applicants argue:

a. Applicant argues that acetic acid is added to the reaction solvent and is not removed prior to precipitation. The Examiner agrees and points out that the open "comprising: language of both claims 5 and 12 permits the presence of acetic acid and acetate ions.

b. Applicant argues that the precise temperature employed by Claude is unstated. The Examiner agrees with Applicants and points out that Applicants' temperature overlap the range taught by Claude.

c. Applicant further argues that the temperature employed by Claude corresponds to a bath temperature and not the internal temperature of the cystallization solution. The Examiner agrees with Applicants that this would be a natural assumption but points out that it is not supported by the facts of record.

With regard to the rejection of claims 12-15 Applicants argue:

a. Applicants' argues that Claude is silent with regard to the use of seed crystals and especially A-type crystals. To this the Examiner responds that Claude is not relied upon for the teaching of the use of the seed crystal. Applicant's declaration was unconvincing with regard to distinguishing the claimed A-type crystal from the prior art crystal taught by Claude and is therefore presumed to be present in the prior art crystal.

b. Applicants' further argue (Page 10, 2nd and 3rd paragraphs) that the yield obtained by Mr. Kawahara was lower than that stated by Claude. The Examiner responds that this has no relevance to the issues in this case.

c. Applicants' further present arguments (Page 10, 3rd paragraph – page 11, 2nd full paragraph) based on Prakash. The conditions used by Prakash are not relevant to the issues in this case.

d. Applicants further argue (Page 11, 4th full paragraph) that the temperature in the crystallization vessel was about 23-28°C during evaporation of methanol under vacuum in the Declarant's experiment. The Examiner again points out that Applicants' are making assumptions with regard to the disclosure of Claude which have no basis in the record. In fact, since Claude sets an upper limit on the temperature, it would be just as reasonable to assume that enough heat was supplied to maintain the internal temperature of the solution at a temperature of 40°C.

e. Applicants argue (Page 12, 1st full paragraph) that Tosoh is silent with regard to the crystallization of neotame. The Examiner agrees. Tosoh, however, is not relied upon for such teaching.

f. Applicants' further argue that Aspartame and neotame are different compounds and would have different properties. While this is true, the properties of neotame and aspartame would be expected to be very similar. The extent of overlap in their structure is extremely great. So much so that one of ordinary skill in the art would expect that they would display very similar crystallization behavior.

g. The Examiner acknowledges, and agrees with, Applicants' submission that neither chemical reactivity nor physiological properties are relevant to the considerations of crystallization.

h. Applicant further argues that the physical properties of aspartame and neotame such as molecular weight differ and that Tosoh itself supports this argument since seeding by Tosoh produces crystals having a greater width to length ratio. The Examiner agrees with Applicants that the physical properties of neotame and aspartame differ and that seeding is performed by Tosoh for the purposes of emphasizing a different crystalline characteristic from that instantly desired. This, however, does not detract from the teaching by Tosoh that the characteristics of a product crystal can be controlled by the addition of seed crystals having the desired characteristics.

i. Applicants assert that neotame crystals having a greater width to length ratio are not formed. The Examiner points out that there no facts on record to support or disprove this assertion.

j. Applicant asserts that Claude contains no disclosure of A-type crystals. As discussed above, however, the Examiner points out that Applicant has not convincingly demonstrated that Claude does not disclose A-type crystals since the presentation of selected peaks is unconvincing.

Applicant's arguments filed 28 June 2002 have been fully considered but they are not persuasive for the reasons indicated above.

Claim Rejections - 35 USC § 112

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

14. Claims 5-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 5 and 12 recite selected peak values as characteristic of the x-ray diffraction pattern of a particular crystalline form of N-[N-(3,3-dimethylbutyl)-L—aspartyl]-L-phenylalanine methyl ester. This is an insufficient means of characterization of the x-ray diffraction spectrum which renders claims 5 and 12 and their dependents indefinite. Applicants should amend these claims refer to the figure of the x-ray diffraction of the claimed crystalline compound.

Conclusion

15. Claims 5-15 are outstanding. Claims 5-15 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul A. Zucker whose telephone number is 703-306-0512. The examiner can normally be reached on Monday-Friday 7:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on 703-308-4532. The fax phone numbers for the organization where this application or proceeding is assigned are

703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Paul A. Zucker
Patent Examiner
Technology Center 1600
September 17, 2002

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